

# PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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FORMALITIES:

PAT. OFF:

ON DB:

CASE NO:

PA0363-PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY

(PCT Rule 71.1)

Date of mailing  
(day/month/year)

03.11.2005

Applicant's or agent's file reference

PA0363-PCT

## IMPORTANT NOTIFICATION

International application No.

PCT/GB2004/003247

International filing date (day/month/year)

28.07.2004

Priority date (day/month/year)

29.07.2003

Applicant

AMERSHAM BIOSCIENCES UK LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:



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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PA0363-PCT		<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/GB2004/003247		International filing date ( <i>day/month/year</i> ) 28.07.2004		Priority date ( <i>day/month/year</i> ) 29.07.2003
International Patent Classification (IPC) or national classification and IPC G01N1/30, G01N21/64, G01N33/487				
Applicant AMERSHAM BIOSCIENCES UK LIMITED et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> <i>sent to the applicant and to the International Bureau</i> a total of 6 sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input checked="" type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  02.02.2005		Date of completion of this report  03.11.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer  Michalitsch, R  Telephone No. +49 89 2399-2930		

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INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY

International application No.  
PCT/GB2004/003247

IAP20 Rec'd PCT/GB 19 DEC 2005

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
    - ☐ international search (under Rules 12.3 and 23.1(b))
    - ☐ publication of the international application (under Rule 12.4)
    - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-38 as originally filed

Claims, Numbers

1-36 as originally filed

Drawings, Sheets

1/10-10/10 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
  - ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☒ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
  - ☐ the description, pages
  - ☒ the claims, Nos. 1-35
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 2,3

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 2,3 are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/GB2004/003247

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	5-32, 34-36
	No: Claims	1,4,33
Inventive step (IS)	Yes: Claims	
	No: Claims	1,4-36
Industrial applicability (IA)	Yes: Claims	1,4-36
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

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**Box No. VIII Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)

PCT/GB2004/003247

The amendments introduced by the set of claims filed in response to the Written Opinion of the International Search Authority (WOISA) are considered to go beyond the disclosure of the application as originally filed.

The wording "given time" and "different time" have a much broader scope than "first" and "second". The subject matter of the claims hence covers a substantially broader scope than the original claim set.

Furthermore, the applicants have not indicated any passages in the description that would provide a basis for the amendments carried out.

Furthermore the basis for the amendments is not **immediately obvious** from the originally filed claim set nor the description.

In consequence, this report has been established as if the amendments had not been filed (Rule 70.2c PCT).

In conclusion this report is established on the basis of the originally filed claims and the opinion set out in the WOISA is maintained across the whole range.

**Re Item III.**

The subject matter of claims 1 to 4, and 33 is unclear insofar as the term "first time", "first image" and "second time" are merely used as labels. However, these terms must not be used as labels, but relate exclusively to chronological orders or rows. A first time always has to come before a second time. Consequently, claim 2 does in no way restrict the scope of the claim it depends on and claims 2 and 3 are not subject of the provisional examination.

- Furthermore, the meaning of "less capable of identifying" is unclear insofar as it leaves the reader in doubt whether known methods of the prior art fall under the scope of the claim, or not. E.g. all fluorescent markers, which are commonly used in the field, fall under the definition of claim 1, since a fluorescent marker is only capable to identify e.g. a cell nucleus when irradiated with an appropriate wavelength. When the irradiation source is switched off, the dye naturally is less capable of providing this function.



- Furthermore the fluorescence exhibits a time decay etc. Hence such dyes and a broad range of other markers inherently exhibit temporally varying signals as also claimed in claim 5.
- Claim 4 appears to contradict claim 1 insofar as the marker is added only after the recording of the first image. If claim 1 is seen under the light that the marker is not necessarily initially present, this implies that the claim actually is directed towards a standard laboratory method, such as background removal in images. Anyway, such methods belong to the mental furniture and the daily practice of a skilled person and would not even require the citation of relevant prior art in order to state that claimed subject matter lacks an inventive step in the sense of Art. 33(3) PCT.

In conclusion, the claims 1 to 4, and 33 do not fulfill the requirements of Art. 6 PCT. **The definition of the subject matter in the independent claims is so broad that virtually all prior art documents disclosing image subtraction methods appear to anticipate the claimed subject matter or render it obvious.**

**Re Item V.**

- 1 The following documents are referred to in this communication:
  - D1 : US 5 347 139 A (BARKER DAVID L ET AL)
  - D2 : US 4 389 670 A (CASE ARTHUR L ET AL)
  - D3 : PATENT ABSTRACTS OF JAPAN vol. 0082, no. 54 (P-315)  
& JP 59 126529 A (FUJI SHASHIN FILM KK)
  - D4 : DE 100 65 632 A (SMTECH BIOVISION HOLDING AG EC)
  - D5 : EP 0 401 077 A (BIOLOG VISIONS)

**2 INDEPENDENT CLAIM 1**

- 2.1. D2, which is considered to represent the most relevant state of the art, discloses a method for localizing, detecting and quantifying macromolecules, in particular biological materials, with an imaging system (abstract, col.2 lines 50-60) using radioactive or fluorescent markers for generating spacial definitions or providing for background removal etc. (D2, col. 5, lines 6-35).

The difference between the characterising features of D2 and the subject matter of the present application and claims 1 and 33, in particular, consists in the precise definition of the first and second times for taking the images and the use of the same marker in both images (although this reversed in claim 4)

The technical problem to be solved could consequently be seen in the need for minimizing the time/labour effort invested for generating a spatial definition of the biologic entitle.

As already argued above, under the discussion of lack of clarity, the ISA takes the viewpoint that the skilled person is aware of such a procedure, since it comes with his customary practice. As set out before, just the switching off of a light source would provide for the same effect.

**Therefore the present independent claims and the claim set as a whole appears to lack an inventive step, in breach of Art. 33(3) PCT.**

Related arguments also apply with respect to combinations of D2 with the available prior art, and D5 in particular.

D5 describes methods of removing background and noise from images to generate dynamic spatial information of labelled objects, relying on the comparison and subtraction of sequentially recorded images (D5, col.4 lines 33-48, col. 18. lines 18-44; col. 19, lines 25-51 as well as claims 16 and 17).

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